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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/145,180	09/01/1998	JIA-HE LI	23356-M5	5665

7590

05/24/2002

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EXAMINER

WANG, SHENGJUN

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 05/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/145,180

Applicant(s)

LI ET AL.

Examiner

Shengjun Wang

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on March 4 & 6, 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 184-233 is/are pending in the application.
- 4a) Of the above claim(s) 193-195, 197-206, 208, 214, 215 and 217-233 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 184-192, 207, 209-213 and 216 is/are rejected.
- 7) ☒ Claim(s) 196 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 22.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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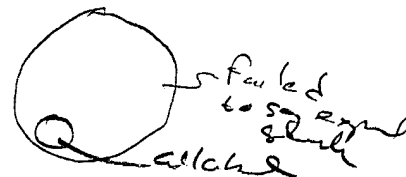
### DETAILED ACTION

Receipt of applicants' remarks submitted March 4 and 15, 2002 is acknowledged.

#### *Claim Objections*

1. Claim 196 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

#### *Claims Rejections 35 U.S.C. - 103*



1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 184-192, 196, 207, 209-213 and 216 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weltin et al. (AT of page 5, IDS paper No. 3) in view of Banasik et al. (AH, IDS paper No. 4), Suto et al (AR, IDS paper No. 4) and Endres et al. (AT of page 2, IDS paper No. 3) for reasons essentially the same as set forth in the prior office action. Specifically, since optimization of PARP inhibiting activity of isoquinoline derivatives by amino and/or nitro substituents is known in the art, a person with ordinary skill in the art would have been reasonably expected to optimize of PARP inhibiting activity of 6(5H)-phenanthrindinone by adding amino and/or nitro group to 6(5H)-phenanthrindinone. Further, note that 2-nitro substituted 6(5H)-phenanthrindinone disclosed by Banasik et al. would read on the compounds employed in the claimed invention.

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Weltin et al. (AT of page 5, IDS paper No. 3) teach that 6(5H)-phenanthrindinone, an isoquinoline derivative, is a potent inhibitor of poly(ADP-ribose) polymerase (PARP). See the abstract and Figure 1.

Weltin et al. do not teach expressly the employment of a substituted 6(5H)-phenanthrindinone, i.e., 10-amino-2-nitro-6(5H)-phenanthrindinone, for treating ischemia.

However, Endres et. al. (AT of page 2, IDS paper No. 3) teach a method of treating ischemia by inhibition of PARP activity. See page 1144, third paragraph. Suto et al. (AR, IDS paper No. 4) teach a method of optimization of PARP inhibiting activity of isoquinoline derivatives. The method comprising adding various substituents, e.g., nitro and amino groups, to isoquinoline derivatives. Isoquinoline derivative with substituent at 5 position give optimal results. See, page 109, table 1. Banasik et al teaches that 2-nitro substituted 6(5H)-phenanthrindinone have more inhibition activity against PARP than 6(5H)-phenanthrindinone. ( $IC_{50}$  0.35  $\mu$ M). See page 1573 right column, compound No. 3.

Therefore it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ substituted 6(5H)-phenanthrindinone, e.g., 10-amino-2-nitro-6(5H)-phenanthrindinone for treating ischemia

#### ***Response to the Arguments***

Applicants' response submitted March 4<sup>th</sup> and 15<sup>th</sup>, 2002 have been fully considered, they are persuasive with respect to the elected compound, and not persuasive with respect to other issue as discussed below.

Applicants' arguments that the cited references merely provide an invitation to further experimentation for the elected compound 10-amino-2-nitro-6(5H)-phenanthrindinone

persuasive, therefore, subject matter in claim 196 would be allowable. Particularly, the cited reference does not provide sufficient suggestion or motivation to arrive the particular compound 10-amino-2-nitro-6(5H)-phenanthrindinone, considering the number of possible isomers.

However, the broad claims are properly rejected on the ground of record as discussed above.

(Note applicants' citing that Banasik reference teaches "10-amino-2-nitro-6 (5H)-phenanthrindinone" is believed to be a typo of "2-nitro-6 (5H)-phenanthrindinone")

Applicants erred in stating "Endres reference only relates to use of 3-aminobenzamide." Endres reference teaches generally that "inhibition of PARP enzyme activity promote s resistance to ischemic brain injury" See page 1144, paragraph 3. It would have been prima facie obvious for one of ordinary skill in the art to employ PARP inhibitor for treatment of ischemia.

Applicants' statement that "The examiner appears to believe that phenanthrindinone is a derivative of isoquinolinone..." is improper. Note "phenanthrindinone is a derivative of isoquinolinone" is not based on the examiner's understanding but based on the general knowledge in the art. For example, Banasik reference lists 2-nitro substituted 6(5H)-phenanthrindinone as derivative of isoquinolinone. See, page 1573, left column, under the Results, item 1, Isoquinoline derivatives.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (703) 308-4554. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Examiner



Shengjun Wang

May 22, 2002

RUSSELL TRAYERS  
PRIMARY EXAMINER  
GROUP 1200